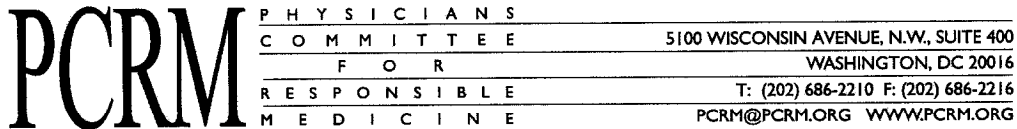


201-15351



June 14, 2004

Michael O. Leavitt, Administrator  
US Environmental Protection Agency  
Ariel Rios Building  
Room 3000, #1101-A  
1200 Pennsylvania Avenue, NW  
Washington, DC 20460

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Subject: Comments on the HPV test plan for Eicosenoic Acid, Methyl Ester, (Z)-

Dear Administrator Leavitt:

The following are comments on the test plan for eicosenoic acid, methyl ester, (Z)- (EA, CAS # 76899-35-9) for the HPV program, submitted by Crompton Corporation. These comments are submitted on behalf of the Physicians Committee for Responsible Medicine, People for the Ethical Treatment of Animals, the Humane Society of the United States, the Doris Day Animal League, and Earth Island Institute. These animal, health and environmental protection organizations have a combined membership of more than ten million Americans.

The test plan proposes to conduct **all mammalian toxicity SIDS endpoints, including the LD50 test, which is no longer an accepted test method.** As the test plan proposes tests that will kill, at minimum, 760 animals, it is imperative that Crompton ensures that it has taken all measures to justify testing, as recommended by the EPA (please see <http://www.epa.gov/chemrtk/ceoltr2.htm>).

First and foremost, EA is a fatty acid. As such, catabolism of fatty acids is a well-documented metabolic process (Champe & Harvey, 1994) in animals and humans. Research has established that mammals have enzyme systems capable of metabolizing short, medium, long, and branch chain fatty acids. The metabolic pathway is the same for all chain lengths and does not distinguish between saturated and unsaturated fatty acids. The metabolic product for even numbered fatty acids is acetyl-CoA (or acetate). Eicosenoic acid falls within the molecular range of fatty acids normally metabolized by animals and humans, and has no structural characteristic that would indicate that it requires toxicity testing.

Moreover, this test plan is clearly lacking critical details and because of this, the EPA should reject it in full. For example, the Introduction, which should detail uses, human exposures, and manufacture processes, consists of one sentence: "The substance is used as ??????????" [sic]. There has been no attempt to use physicochemical data or behavior to bridge mammalian toxicity data with other similar chemicals, some of which have been a part of previous test plans submitted by the Pine Chemicals Association, the American Petroleum Institute, and Dow Chemical Company, to name a few. Data from other fatty acids and related substances could clearly help complete a picture of EA's toxicity, and is likely to be readily available in the public domain.

In fact, no consideration appears to have been given to the overall knowledge base of EA. It is imperative that basic use and exposure information be collected first, before proposing any animal testing. As stated in the above-referenced EPA letter to HPV sponsors:

“In analyzing the adequacy of existing data, participants shall conduct a thoughtful, qualitative analysis rather than use a rote checklist approach. Participants may conclude that there is sufficient data, given the totality of what is known about a chemical, including human experience, that certain endpoints need not be tested.... As with all chemicals, before generating new information, participants should further consider whether any additional information obtained would be useful or relevant.”

Furthermore, a number of fatty acids and related compounds are listed on the FDA GRAS list, and are approved and used as food additives and dietary supplements. In fact, EA has been detected in olive oil (Artaud *et al.*, 2003). Any new proposed testing should be evaluated in the light of these facts and other data. If EA or similar chemicals are considered GRAS, the EPA suggests that

“In analyzing the adequacy of screening data for chemicals that are substances Generally Recognized as Safe (GRAS) for a particular use by the Food and Drug Administration (FDA), participants should consider all relevant and available information supporting the FDA's conclusions. Participants reviewing the adequacy of existing data for these chemicals should specifically consider whether the information available makes it unnecessary to proceed with further testing involving animals....”

If, after these measures have been exhausted, Crompton determines that animal testing is still warranted, more specificity as to the exact method is needed. First, any acute testing should follow recently recommended *in vitro* dose-finding and Up-and-Down procedures to ensure the minimum number of animals are killed. For the genotoxic endpoints, human cells should be used.

Thank you for your attention to this issue. I look forward to a prompt and favorable response to our concerns. I can be reached at 202-686-2210 ext. 335 or via email at [kstoick@pcrm.org](mailto:kstoick@pcrm.org).

Sincerely,

Kristie Stoick, MPH  
Research Analyst

Chad B. Sandusky, PhD  
Director of Research

## References

Artaud OD, Pinatel J, Durbec JP, and Guerere M. Triacylglycerol and fatty acid composition of French virgin olive oils. Characterization by Chemometrics. *Agric. Food Chem.* 51(19): 5723-31. 2003.

Lippincott's Illustrated Reviews: Biochemistry by Pamela C. Champe and Richard A. Harvey. 1994.